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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Toshio Doi

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2292 7590 05/27/2009  
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EXAMINER

KEMMERER, ELIZABETH

ART UNIT

PAPER NUMBER

1646

NOTIFICATION DATE

DELIVERY MODE

05/27/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/571,511	<b>Applicant(s)</b> DOI ET AL.	
	<b>Examiner</b> Elizabeth C. Kemmerer, Ph.D.	<b>Art Unit</b> 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 1-11 and 15-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12-14, 25-29 and 31 is/are rejected.
- 7) ☒ Claim(s) 30 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Status of Application, Amendments, And/Or Claims***

The amendment of 17 February 2009 has been entered in full. Claims 1-11 and 15-24 remain withdrawn from consideration. Claims 12-14 are amended. Claims 25-31 are new. Claims 12-14 and 25-31 are under examination.

### ***Withdrawn Objections And/Or Rejections***

The requirement for a new title as set forth at p. 3 of the previous Office action (mailed 17 November 2008) is *withdrawn* in view of the amended title (17 February 2009).

The rejection of claims 12-14 under 35 U.S.C. § 101 regarding non-statutory subject matter as set forth at pp. 3-4 of the previous Office action (mailed 17 November 2008) is *withdrawn* in view of the amended claims (17 February 2009).

The rejection of claims 12-14 under 35 U.S.C. § 101 regarding non-statutory subject matter as set forth at pp. 3-4 of the previous Office action (mailed 17 November 2008) is *withdrawn* in view of the amended claims (17 February 2009).

The rejection of claims 12-14 under 35 U.S.C. § 102(b) as being anticipated by Monia et al. as set forth at pp. 4-5 of the previous Office action (mailed 17 November 2008) is *withdrawn* in view of the amended claims (17 February 2009).

The rejection of claims 12-14 under 35 U.S.C. § 112, second paragraph, as set forth at pp. 5-6 of the previous Office action (mailed 17 November 2008) is *withdrawn* in view of the amended claims (17 February 2009).

**35 U.S.C. § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12, 13, 25, 27-29, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al. (1999, Biochem. J. 342:231-238) in view of Yamanouchi et al. (WO 00/73791, published 07 December 2000).

Please note that Yamanouchi et al. (WO 00/73791, published 07 December 2000), a document in Japanese, has an English language equivalent document in Yamagouchi et al., US 6794154.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Huang et al. disclose a method of contacting a test agent (AGE) with a biological sample (NRK-49F cells), and determining the level of STAT3 in the biological sample in comparison to the level of expression in a control sample (NRK-49F cells which were not contacted with AGE). See p. 235, Figure 4. Expression was determined at the protein level by Western Blotting.

Huang et al. do not specifically teach that a decrease in expression indicates that the agent is effective in the prevention and/or treatment of proliferative diseases causing sclerosis or that the agent is effective in inhibiting the increase of cellular matrix.

However, Huang et al. appreciated the link between AGE, STAT3 expression, and diabetic nephropathy, which is a disease causing sclerosis characterized by extracellular matrix accumulation. See Abstract and 1<sup>st</sup> two paragraphs of Introduction at p. 231. Given that the skill level in the drug discovery arts is very high, the person of ordinary skill in the art would have been motivated to use the link between increased STAT3 levels and diabetic nephropathy to screen for potential drug candidates that would lower STAT3 levels, thus treating the disease and inhibiting increased extracellular matrix.

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Such a basic screening method is taught by Yamanouchi et al., who observed that FABP expression is decreased in urine or renal tissues preceding fibrotic diseases such as diabetic nephropathy, and use that observation to devise a drug screening system to identify candidate drugs that would up-regulate FABP expression to prevent and/or treat the disease and inhibit extracellular matrix accumulation. Yamagouchi et al. used renal cells and tissues for their assays.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Huang et al. to screen for agents that decrease STAT3 expression in order to identify agents that would prevent/treat diabetic nephropathy and inhibit extracellular matrix accumulation with a reasonable expectation of success. Yamagouchi et al. is evidence that such was well within the ordinary level of skill in the art. Moreover, it is noted that the three-pronged test for obviousness (i.e., suggestion, motivation and expectation of success in the prior art) is one of a number of rationales that can be used to support a finding of obviousness, as established by KSR. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396) (available at <http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>). Rather, an additional rationale for the instant finding of obviousness is that the claims would have been obvious because a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. Thus, the artisan would still at least be motivated to use a basic screening method such as that taught by Yamagouchi et al. to look for inhibitors of STAT3 expression based on the disclosure of Huang et al. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al. (1999, Biochem. J. 342:231-238) in view of Yamanouchi et al. (WO 00/73791, published 07 December 2000) as applied to claims 12, 13, 25, 27-29, and 31 above, and further in view of Cohen et al. (US 5,908,925; issued 01 June 1999).

Again, please note that Yamanouchi et al. (WO 00/73791, published 07 December 2000), a document in Japanese, has an English language equivalent document in Yamagouchi et al., US 6794154.

As discussed above, Huang et al. (1999) teaches that AGE increases STAT3 production and leads to sclerotic diseases such as diabetic nephropathy. Taken with Yamagouchi et al., the references teach a method of screening for agents effective in preventing/treating proliferative diseases causing sclerosis such as diabetic nephropathy or inhibiting extracellular matrix production. The method comprises screening for decreased STAT3 production in renal cells upon exposure to the test agent in comparison with a control.

Neither reference specifically teaches a method of screening for agents that inhibit expression of Type IV collagen.

However, Cohen et al. teach that diabetic nephropathy was known to be characterized by increased extracellular matrix comprising collagen IV. See col. 1, 1<sup>st</sup> paragraph. Therefore, Cohen et al. constitutes evidence that an agent that prevents/treats diabetic nephropathy would also indirectly inhibit collagen IV production.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Huang et al. to screen for agents that decrease STAT3 expression in order to identify agents that would prevent/treat diabetic nephropathy and inhibit extracellular matrix accumulation with a reasonable expectation of success. Yamagouchi et al. is evidence that such was well within the ordinary level of skill in the art. Cohen et al. is evidence that such a screening method

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would also identify agents that inhibited type IV collagen production. Thus, combining the teachings of the prior art would have been tantamount to combining prior art elements according to known methods to yield predictable results.

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al. (1999, Biochem. J. 342:231-238) in view of Yamanouchi et al. (WO 00/73791, published 07 December 2000) as applied to claims 12, 13, 25, 27-29, and 31 above, and further in view of Wang et al. (2002, Diabetes 51:3505-3509).

Again, please note that Yamanouchi et al. (WO 00/73791, published 07 December 2000), a document in Japanese, has an English language equivalent document in Yamagouchi et al., US 6794154.

As discussed above, Huang et al. in view of Yamagouchi et al. teach a method of screening for agents effective in preventing/treating proliferative diseases causing sclerosis such as diabetic nephropathy or inhibiting extracellular matrix production. The method comprises screening for decreased STAT3 production in renal cells upon exposure to the test agent in comparison with a control.

Neither reference specifically suggests using mesangial cells. However, Wang et al. teach that STAT3 is elevated in mesangial cells upon exposure to high glucose in another model for the study of diabetic nephropathy. See p. 3505, abstract; p. 3507, Figure 2.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Huang et al. by using a screening



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method as taught by Yamagouchi et al. and mesangial cells as taught by Wang et al. with a reasonable expectation of success, since such would have been tantamount to combining prior art elements according to known methods to yield predictable results.

### ***Claim Objections***

Claim 30 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

### ***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (571) 272-0874. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D. can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ECK/  
21 May 2009

/Elizabeth C. Kemmerer/  
Elizabeth C. Kemmerer, Ph.D.  
Primary Examiner, Art Unit 1646